

Draft Guidance on Amitriptyline Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Amitriptyline Hydrochloride

Form/Route: Tablet/Oral

Recommended study: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 25 mg
Subjects: Healthy males and nonpregnant females, general population
Additional comments:
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2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: 25 mg
Subjects: Healthy males and nonpregnant females, general population
Additional comments:
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Analytes to measure (in appropriate biological fluid): Amitriptyline, and its active metabolite, nortriptyline, in plasma

Bioequivalence based on (90% CI): Amitriptyline

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, please submit (i) individual and mean concentrations, (ii) individual and mean pharmacokinetic parameters, and (iii) geometric means and ratios of means for AUC and C_{max}.

Waiver request of in-vivo testing: 10 mg, 50 mg, 75 mg, 100 mg, and 150 mg based on (i) acceptable bioequivalence studies on the 25 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

Dissolution test method and sampling times:

Please note that a Dissolution Methods Database is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.